1996 ASHG PRESIDENTIAL ADDRESS
Toward the 21st Century

Charles J. Epstein

Department of Pediatrics, University of California, San Francisco

Three years ago, when I completed my term as editor of *The American Journal of Human Genetics,* I wrote an editorial broadly titled "Seven Momentous Years," which outlined what had happened during the 7 years I was responsible for the *Journal* (Epstein 1993). On rereading this editorial, I was amazed at what was included in the list of the scientific accomplishments of the period from 1987 to 1993:

- Positional and functional cloning of over 25 disease genes
- Discovery of the triplet-repeat diseases and resurrection of anticipation
- Autosomal imprinting and imprinting diseases in man
- First uses of gene therapy
- Mouse models by transgenesis and homologous recombination
- Mathematical and physical approaches to linkage analysis
- mtDNA diseases
- Human Genome Project
- cDNA cloning and sequencing
- Forensic applications of DNA analysis
- Tumor-suppressor genes
- Microdeletion syndromes
- Peculiarities of the sex chromosomes
- Evolutionary conservation of the genome
- Evolution and migration of human populations
- New methods for prenatal screening and diagnosis
- Analytical techniques and instrumentation
- Concern with legal and ethical issues

All of these things largely came to fruition in a period of roughly 7 years. And, look at just some of what has happened in the 3 years that have gone by since the editorial was written:

- Over 60 disease genes have been identified by positional cloning, and the total number of genes cloned by any means is much greater.
- Full genome searches for the analysis of complex human diseases are becoming commonplace.
- New classes of disease genes have been appreciated—transcription factors, transporters, channels, fibroblast growth-factor receptors, and, most recently, the helicases.
- The first human *HOX* gene disorder has been identified and joins the *PAX* and *SOX* diseases.
- The mapping of the human genome is well along, and major sequencing is beginning.
- The number of genomic markers is becoming vast—in the tens of thousands.
- Virtually every gene that you can think of has been knocked out in the mouse.
- Powerful new techniques of molecular cytogenetics have been developed—24-color chromosome paints, competitive genomic hybridization.
- Triple-marker screening for cytogenetic disorders has been greatly expanded.

We can only guess where we will be 4 years from now, when the 20th century ends and the 21st century and the new millennium begin.

Not Everyone Loves Human Genetics

From all that I have said to this point, we have every reason to be proud of our accomplishments and to be optimistic about the future of human genetics. However, if I learned nothing else from the events that began on June 22, 1993, when I received an unwelcome gift from the Unabomber, it was that not everyone believes that genetics is God's gift to mankind. I was, as you might imagine, quite interested in what the Unabomber, or "FC," as he called himself, had to say about genetics when his infamous manifesto, "Industrial Society and Its Future," made its appearance (FC 1995). In truth, the Unabomber had relatively little to say on the subject—and nothing about me personally—but what he did say certainly did get my attention.

In the section entitled "The 'Bad' Parts of Technology Cannot Be Separated from the 'Good' Parts," he tells us the following:

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Address for correspondence: Dr. Charles J. Epstein, Department of Pediatrics, Box 0748, University of California, San Francisco, CA 94143-0748. E-mail: cepst@itsa.ucsf.edu

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> Suppose . . . that a cure for diabetes is discovered. People with a genetic tendency to diabetes will then be able to survive and reproduce as well as anyone else. Natural selection against genes for diabetes will cease and such genes will spread throughout the population. . . . The same thing will happen with many other diseases susceptibility to which is affected by genetic factors (for example, childhood cancer), resulting in massive genetic degradation of the population.
>
> The only solution will be some sort of eugenics program or extensive genetic engineering of human beings, so that man in the future will no longer be a creation of nature, or of chance, or of God (depending on your religious or philosophical opinions) but a manufactured product.
>
> If you think that big government interferes in your life too much NOW, just wait till the government starts regulating the genetic constitution of your children. Such regulation will inevitably follow the introduction of genetic engineering of human beings, because the consequences of unregulated genetic engineering would be disastrous.

He then goes on in the following vein:

> The only code of ethics that would truly protect freedom would be one that prohibited ANY genetic engineering of human beings, and you can be sure that no such code will ever be applied in a technological society. . . . Inevitably, genetic engineering will be used extensively, but only in ways consistent with the needs of the industrial-technological system. . . . And, as nuclear proliferation has shown, new technology cannot be kept out of the hands of dictators and irresponsible third-world nations. Would you like to speculate about what Iraq or North Korea will do with genetic engineering.

A potent image, indeed!—Iraq and genetic engineering—although I dare say that Saddam Hussein has other things on his mind just now.

The Unabomber Is Not Alone

The Unabomber has been characterized by some as being a Luddite, a person who wishes to turn back the clock and to return to some ill-defined time before the advent of technology. However, it is not my intention to analyze either the philosophy or the genetics of the Unabomber, and none of us, I dare say, would regard him as an expert in either field. Nevertheless, I do think that it is worth pointing out that the sentiments expressed in his manifesto are *not* out of line with much that has been said or written by less disturbed minds. The Unabomber is playing to fears and concerns that already exist. Just consider the images on two recent periodical covers. On one, from *Technology Review* (1996), with the caption "Misusing Genetics," the DNA helix replaces the serpent in the Garden of Eden; on the other, from *The Economist* (1996), with the caption "The Genetic Illusion," man is shown ensnared in fetters composed of DNA helices.

If all of the criticisms of genetics and its potential applications were at the level of the Unabomber's manifesto and similar types of writings, I would be concerned but would not be deeply troubled. However, criticisms of geneticists and what they do and have done come from quarters much closer to home. For the most part, they have been particularly leveled at certain clinical applications of genetics, particularly prenatal diagnosis and carrier screening. More than once, whether at a lecture in a medical anthropology course at the University of California, San Francisco (UCSF), or at a public hearing before the California Senate Select Committee on Genetics, I have heard genetic screening and testing referred to variously as racist, sexist, insensitive, and/or just plain misguided.

Gene therapy has certainly not been immune. Quite the opposite. It has conjured up a whole host of concerns and fears of its own. I have even witnessed people in wheelchairs coming to a meeting of the Recombinant DNA Advisory Committee—the RAC—to assert that gene therapy constitutes a form of discrimination against the disabled.

This is, of course, not what any of us involved with such things wants or expects to hear. Perhaps we are naive, but we believe that our intentions are good and that what we are doing has merit. We really think that we are trying to help people, trying to understand how genes affect human life, trying to do research to improve the human condition. What, then, are we doing wrong?

In the *The American Journal of Human Genetics* editorial from which I have already quoted, after giving all of the good news, I went on to write that "[of greater] concern . . . is the public's very real fear of what progress in genetics might bring. It cannot be ignored. The scientific hubris and resulting chaos portrayed in *Jurassic Park,* the history of the eugenics movement in America, the Nazi racial purification schemes which culminated in the Holocaust, and the anti–gene therapy stance of Jeremy Rifkin have all had a negative influence on public thinking about genetic research and what it might lead to" (Epstein 1993, p. 1164). If anything, these sentiments are even more true today than they were 3 years ago.

The Prevalent Distrust of Science

Just over a year ago, John Maddox, the former editor of *Nature,* published a commentary on "The Prevalent Distrust of Science." I would like to share with you some of what he had to say.

> Distrust of science is still alarmingly prevalent, which conflicts with reasonable expectation. Is not the century now drawing to a close most of all remarkable for the technology that now fills our world and for the understanding of that world that has been won since, say, the discovery of the electron in 1897 [or, I would add, since the rediscovery of Mendelian genetics in 1900]?
>
> During that long period, the improvement in the human condition has been immense. . . . In general, science and

> technology have helped to make us healthy, wealthy and wise in a manner and to a degree not foreseen except by a few visionaries such as H.G. Wells. . . . What is now being learned of human genetics . . . will be dramatically reflected in the health of our populations in the decades ahead. (Maddox 1995, p. 435)

I think that most, if not all, of us would agree with this assessment of the contributions of science and technology and, within our own little world, of genetics. "So why," Maddox goes on, "given all of these benefits of health, wealth, and wisdom, to which science has made such important contributions, does there persist the deep distrust of science we see around us? . . . The standard answer is that science and scientists have in the past made exaggerated claims of what innovation will do for the world at large, so that scientists are no longer trusted. . . . The nuclear power saga of the 1950s may be one illustration, molecular genetics is at risk of becoming another" (Maddox 1995, p. 435–436).

However, Maddox points out that there is more to the problem of the public perception of science than just hype. "The general distrust of science has other and more primitive roots. To the extent that science and its applications bring improvements in our lot, they also imply change, and change is never welcome for its own sake. Then this knowledge that I've been extolling is often unwelcome" (Maddox 1995, p. 436).

It is interesting that Maddox couches what he calls "the standard answer"—exaggerated claims—in terms of the past, but, when it comes to genetics, he predicts trouble in the future. Well, I can tell you that the future has already arrived!

Almost a year ago, a Panel to Assess the NIH Investment in Research on Gene Therapy, the so-called Orkin/Motulsky committee, presented its report to the NIH Director's Meeting (Orkin and Motulsky 1995). Among the committee's findings was the following:

> Expectations of current gene-therapy protocols have been oversold. Overzealous representation of clinical gene therapy has obscured the exploratory nature of the initial studies, colored the manner in which findings are portrayed to the scientific press and public, and led to the widely held, but mistaken, perception that clinical gene therapy is already highly successful. Such misrepresentation threatens confidence in the field and will inevitably lead to disappointment in both medical and lay communities. Of even greater concern is the possibility that patients, their families, and health providers may make unwise decisions regarding treatment alternatives, holding out for cures that they mistakenly believe are "just around the corner."

These are strong words, but to the extent that we bear some of the responsibility for the mistrust of the science of genetics, because of our own hyperbole and inflated claims, the prescription is relatively straightforward. As stated by the Orkin/Motulsky committee, "the panel urges gene therapy investigators and their sponsors—be they academic, governmental, private, or industrial—to be more circumspect regarding the aims and accomplishments of clinical protocols when discussing their work with the scientific community, the public, and the media."

It would be nice to believe, as stated in an editorial in *The Economist* (the cover of which I referred to earlier), that it is not the geneticists who are at fault. The trouble is that other people often read too much into what the geneticists do (The Genetic Illusion 1996). However, whereas these other people might indeed read too much into what we do, we do have to be very careful that we do not give them the opportunity to read too much into what we say.

There have been other accusations of excessive hype on the part of the genetics-research community, beyond those leveled by the Orkin/Motulsky committee. Consider the following headline in the Sunday edition of the *San Francisco Examiner:* "Genes Don't Fit the Hype, Say DNA Skeptics" (Davidson 1996). And, what does the article say?

- " 'Enough!' declared disgusted skeptics, who say the much-hyped genetic revolution is mostly that—hype."
- Overemphasis on genes, they charge, has distracted attention from the crucial role of the environment.
- Much of the ballyhooed genetic revolution "is still in the realm of fantasy. It's being grossly oversold."
- "The genetic paradigm is dead."

From my point of view, the business of hype cuts both ways. It has been as much a tool in opposing genetics as it has been in promoting it. These remarks, which, to be fair, represent a reporter's retelling of what was said, are equally as hyperbolic as whatever statements and claims they are intended to contradict. To the extent that they come from within the genetics community, I think that we should be mindful of how destructive such comments can be. They tar many, if not all, of us with a very broad brush. Just as we have to be careful about promising too much, we must also be careful about conjuring up unfounded fears by what we say—or how we say it.

I want to now discuss a small but nonetheless instructive example of what I mean. An instructional videotape and an accompanying teacher's guide aimed at high school and college students has just been produced by a group working at the University of California, San Francisco. I acted as a sometime adviser to the project and even had a cameo role in the tape. Both the tape and guide are quite good, but what I became aware of only after the finished product appeared is the title: "Promise & Perils of Biotechnology: Genetic Testing" (University of California, San Francisco 1996). What bothers me is one word: "perils."

The videotape presents two genetic stories. One is concerned with the presymptomatic testing, for Huntington disease, of a young woman. She turns out, in the end, to carry the gene, and, as the narrator puts it, "taking a test has removed the uncertainty of her situation, with devastating clarity." The other story is about the treatment of familial hypercholesterolemia in a mother and her daughter, and for them the major issue appears to be insurability in the face of an identified predisposition to genetic disease.

So, what is meant by the phrase, "perils of biotechnology"? A description of the videotape, on the back of the teacher's guide, suggests an answer: "As advances in biotechnology allow doctors to use genetic testing to identify more genetic conditions, the information not only helps expectant couples learn about the health of their developing fetus, but also confirm the presence of genetic conditions in children and adults. These findings pose ethical, legal and social dilemmas about how that information should be used."

Are these, then, the "perils"—the ethical, legal, and social dilemmas or issues raised by genetic testing—that all of us have come to know by the acronym of "ELSI"? There is certainly no question that presymptomatic testing for Huntington disease, or breast cancer, or the short QT syndrome, or Alzheimer disease raises a large number of important and difficult issues that many of you are grappling with—privacy and confidentiality, insurability, employability, stigmatization, responsibility to other family members, and more. The problems are real! They are here now! And they require our serious attention! But, are these problems "*perils*"—a term which, to my ear, at least, has a very ominous sound? Perhaps that is, in fact, the intention—to raise public consciousness about the ELSI issues by equating biotechnology or genetic testing with danger (one of the definitions of the term "peril"). I suppose that there are some who would argue that way, but I do not believe that this is the best way to deal with the problem. Certain words can take on a life of their own and convey meanings that we really hadn't intended. and I think that "peril" is such a word.

Now, some of you might object to this semantic analysis, as merely being an attack on a straw man. After all, the purpose of the title is to attract people to use the videotape. "Promise and Perils" does have a nice alliterative ring about it, and I would suspect that whoever coined it wasn't really trying to make it sound ominous. But I want to pursue the issue a bit further, with another example in which I feel that the semantics and what lies behind them are of real importance.

In the *Federal Register* of March 14, 1996, a notice appeared, the summary of which reads, in part: "The Food and Drug Administration (FDA) is proposing to classify/reclassify analyte specific reagents (ASR) presenting a low risk to the public health into class I (general controls), and to exempt these class I analyte specific reagents from the premarket notification requirements. FDA is also proposing to designate class I analyte specific reagents as restricted devices under the Federal Food, Drug, and Cosmetic Act, and to establish restrictions on their sale, distribution and labeling. Finally, FDA is proposing that ASR's presenting a high risk be classified into or retained in class III (premarket approval)" (U.S. Food and Drug Administration, Department of Health and Human Services 1996, p. 10484). The point at issue for us is that the FDA's Immunological Devices Panel recommended that "tests to be used to predict genetic disease or predisposition to disease in healthy or apparently healthy individuals are more properly classified into Class II or III and subject to premarket approval" (U.S. Food and Drug Administration, Department of Health and Human Services 1996, p. 10485). In its own gloss on this recommendation, the FDA speaks of regulating "as Class III devices only those ASR's used in tests intended for use in overtly healthy people to identify a genetic predisposition to a dementing disease, or to fatal or potentially fatal medical disorders (for example, cancer or Alzheimer's disease) in situations where penetrance is poorly defined or variable and latency is long (5 years or longer)" (U.S. Food and Drug Administration, Department of Health and Human Services 1996, p. 10486).

Now, what, you may ask, are Class III reagents? Looking through the document in the *Federal Register*, we find them variously referred to as

- ASR's presenting a high risk to public health
- [Reagents whose] use presents particularly high risks
- Serious health risks [are] associated with their use or in the class of test in which the ASR is being used. These include active ingredients used in tests intended to diagnose potentially fatal contagious infections (for example, HIV or tuberculosis) or intended to safeguard the blood supply. (U.S. Food and Drug Administration, Department of Health and Human Services 1996, p. 10486)

Although the Immunological Devices Panel recommended Class III status for DNA probes used for presymptomatic diagnosis, the FDA itself had some real reservations about the logic of this approach. "FDA is not certain that making a distinction among tests that directly identify genetic material (i.e., deoxyribonucleic acid (DNA), which the Panel recommended for class II or III) as opposed to transcribed genetic material (mRNA) or gene products (proteins and posttranslationally modified proteins) which the Panel recommended for class I, provides a meaningful basis for differing regulatory treatment of ASR's that are used to develop these tests" (U.S. Food and Drug Administration, Department of Health and Human Services 1996, p. 10486).

So, why did the Immunological Devices Panel make its recommendation concerning human DNA reagents? In its report (U.S. Food and Drug Administration, Department of Health and Human Services 1996), the panel cited two types of risks: First, there are the "general risks: variable quality, inappropriate labeling, use by persons without adequate qualifications; clinicians ordering test may be unaware that the clinical performance characteristics of the tests have not been independently reviewed by FDA" (U.S. Food and Drug Administration, Department of Health and Human Services 1996, p. 10485). True enough, but then there are supposedly what are considered unique risks—"the panel also identified a subset of ASR's whose use posed unique risks to public health because of the substantial clinical impact of the information generated using these devices" (U.S. Food and Drug Administration, Department of Health and Human Services 1996, p. 10485).

So now we have it—the high risk to the public health, in the category of risks posed by reagents designed to safeguard us against infectious diseases and to protect the blood supply, derives from "the substantial clinical impact of the information." INFORMATION!!! Information is risky!!! Frankly, the notion boggles the mind!

Once again, there is a kernel of truth behind the terminology. As more and more disease genes and predisposition-to-disease genes are being cloned, new DNA diagnostic reagents are being introduced daily into research and clinical practice. Many of these are indeed what the FDA calls "home brews," tests developed in research laboratories rather than in the traditional pharmaceutical manner, and there are, of course, issues with regard to quality of the reagents, accuracy of tests, and qualifications of the clinicians using them. This is true for all reagents used in medical testing. It is also true that the results from many of the genetic tests which are performed do have a substantial clinical impact. But I do not believe that defining genetic information as a unique risk to the public health is the way to approach the problem. Doing so serves only to increase public apprehension about genetics and geneticists and will, I believe, inhibit both research and practice. That the public needs protection is without question, but implementing an unduly stringent FDA regulation is not the way to provide it.

I want to return one last time to the Maddox commentary I was quoting from before. He tells the following story: "A panel of parliamentarians gathered to discuss the legislative position on genetics and genetic manipulation in their countries. A woman member of the German Bundestag, and a representative of the Green Party, spoke clearly and intelligently and said this: 'You must understand that we Greens believe that to represent the nature of human beings by a description of their genes undermines their dignity as human beings. We shall oppose in the Bundestag any legislation that condones research in human genetics' " (Maddox 1995, p. 437).

Maddox (1995) springs to the defense of the geneticists in a way that I think we would all applaud.

> This implacable position is arresting. It also succeeds in misrepresenting the position of the research community. Broadly speaking, geneticists themselves are deeply suspicious of genetic determinism—the assertion that a person is determined almost exclusively by the genes there happen to be in his or her genome. To their credit, geneticists have also been among the first to draw attention to the respects in which the rapid development of their field is likely to create social problems, chiefly by the use of genetic diagnosis as a basis for discrimination between individuals, mainly in employment and insurance. But evidently the geneticists will win no credit from the German Greens for their perceptiveness. (Maddox 1995, p. 437)

Why do I tell you this? It is because I believe that we may be running into situations in which opposition to genetic research and genetic testing may be based on similar types of premises. There is a strange resonance for me between the statement of the German Greens and a situation that I encountered as president of the society. A document was prepared by a society Rapid Action Team that dealt with informed consent for genetic research on stored tissue samples. When the draft report came to the society's board of directors for approval, there was considerable consternation about some of the recommendations that were made. And, when it was finally published in the August 1996 issue of *The American Journal of Human Genetics,* the report carried an unusual disclaimer indicating that the statement differs from the proposal submitted to the board by the task force and does not necessarily reflect the views of its members (American Society of Human Genetics 1996). What was all the fuss about?

The crux of the issue was what type of informed consent should be required for genetic or DNA-based research on materials obtained either retrospectively—in other words, from samples *already* obtained for either genetic or other purposes—biopsies, surgical specimens, diagnostic laboratory samples, newborn screening tests, whatever—or prospectively, as part of a study design for either research or diagnostic purposes. The major point of contention had to do with the prospective use of anonymous samples (samples originally collected without identifiers and impossible to link to sources) and anonymized samples (samples initially identified but irreversibly stripped of identifiers). The draft report recommended that, whereas retrospectively obtained anonymous or anonymized samples did *not* require full informed consent for use in research, prospectively obtained anonymous or anonymized DNA samples *should,* even though they could not be traced back to the original source. The stated reason for this (American Society of Human Genetics draft report "Statement on

Informed Consent for Genetic Research," personal communication) was that "in genetic studies that are designed to collect new biological samples from individuals and families, the investigators generally have the opportunity to communicate with potential subjects in advance and involve them in the research by obtaining their informed consent. This should be encouraged, even for the prospective studies in which the samples are collected anonymously." The ASHG board did not accept this formulation, because it was felt that this requirement could have a chilling effect on future research with such samples. The board therefore recommended that such consent not be required for prospectively obtained anonymous or anonymized samples, and this is what was ultimately published in the *Journal.*

But the story doesn't end here. Recommendations by the American Society of Human Genetics or its board are just that—recommendations. However, another event was occurring in parallel to the society's drafting of its suggested guidelines, and that was the drafting of the so-called Domenici bill, S. 1898 (U.S. Senate 1996), "To Protect the Genetic Privacy of Individuals, and for Other Purposes."

What did this bill say? First of all, there were a set of what are described as the findings of Congress:

(1) The DNA molecule contains an individual's genetic information, and this information is written in a code that is being rapidly deciphered, sequenced, and understood.
(2) Genetic information is uniquely private and personal information.
(3) Genetic information has been misused resulting in harm to individuals.
(4) The improper use and disclosure of genetic information can lead to significant harm to the individual, including stigmatization and discrimination.
(5) The potential for misuse with respect to genetics is tremendous since genetics transcends medicine. It has the potential to penetrate many aspects of life including employment, insurance, forensics, finance, education, and even one's self-perception.
(6) DNA samples and genetic information should not be collected, stored, analyzed, nor disclosed without the individual's authorization.
(7) A genetic analysis of an individual's DNA provides information not only about an individual, but also about that individual's parents, siblings and children, potentially infringing on individual and family privacy.
(8) Because of its unique nature, DNA can be linked to a single identifiable individual, regardless of whether identifiers are limited to a DNA sample.
(9) Existing legal protections for genetic information are inadequate to ensure genetic privacy.
(10) Uniform rules for the collection, storage and use of DNA samples and genetic information obtained from such samples are needed both to protect individual privacy and to permit legitimate genetic research. (U.S. Senate 1996, sec. 2)

Although there is a distinctly negative cast to the findings with regard to the past and future uses of genetic information, we would probably agree with several of these findings. Some of the findings, however, seem to be more in the nature of first principles of a sort and constitute the philosophical underpinnings of the bill.

- "Genetic information is uniquely private and personal information."
- "The potential for misuse with respect to genetics is tremendous since genetics transcends medicine."
- "Because of its unique nature, DNA can be linked to a single identifiable individual, regardless of whether identifiers are limited to a DNA sample."

The bill, if it had been enacted, would have spelled serious trouble for genetic research. Consider the following provisions:

- A DNA sample is the property of the individual (U.S. Senate 1996, sec. 104).
- The individual shall have the right to order the destruction of the DNA sample (U.S. Senate 1996, sec. 104).
- In the absence of a specific authorization to maintain a DNA sample, DNA samples collected, stored, or analyzed in connection with a research project shall be destroyed upon completion of the project or withdrawal of the individual from the project, whichever occurs first (U.S. Senate 1996, sec. 501[d]).

And what about retrospective analysis? "Any person who, prior to the effective date of this Act, is in possession of a DNA sample shall, prior to performing any genetic analysis on the DNA sample make the disclosures required . . . and obtain a written authorization" (U.S. Senate 1996, sec. 902). There is nothing here or anywhere else in the bill about anonymous or anonymized. Basically, what the bill implies is—no consent, no research! What about all of the archived DNA samples, pathology collections, filter papers, and the rest that have proved so valuable for genetic research? No consent, no research! And one other thing. This Domenici bill is not without teeth. "If the court finds that a person has employed any method, act or practice which the person knew or should have known to be in violation of this Act, the court may require such person to pay a civil penalty of not more than $50,000 for each violation" (U.S. Senate 1996, sec. 802[d]).

The Domenici bill, in the form that I presented, was not acted upon, and it or a new version which is hopefully kinder to genetic research will presumably be taken up by the next Congress. But what have we learned from all of this?

In the report of a workshop sponsored by the National Institutes of Health and the Centers for Disease Control and Prevention, published in *JAMA* as a consensus statement under the title of "Informed Consent for

Genetic Research on Stored Tissue Samples" and known, for short, as "the Clayton report," the following summarizing statement appears: "Society at large must decide how it wishes to weigh the value of respecting persons with the desirability of obtaining socially useful knowledge in a timely manner and of individuals participating in such research, particularly if the personal risks to them are small" (Clayton et al. 1995, p. 1792).

I do not like this formulation very much. To me, it sets up a dichotomy or opposition between respecting persons, on one hand, and the desirability of obtaining socially useful knowledge, on the other. Research and researchers are put into a defensive position from which they must justify their implied incursions into the rights of the persons from whom the DNA ultimately derives. Interpreted in the extreme, the statement really becomes virtually an either/or proposition—if you respect persons, you won't do this research—and this what I believe occurred in the original formulation of the ASHG report and in the drafting of the Domenici bill. If you accept the three premises from the findings of the bill that I already highlighted, along with the proposition that a DNA sample is the property of the individual from whom it came, then it surely must follow that retrospectively obtained DNA samples cannot be analyzed and that no samples can be obtained prospectively, even if anonymous or anonymized, without written consent.

Please don't misinterpret what I am saying. I truly believe that individuals have rights of privacy and of freedom from discrimination and harm that must be protected, and I am supportive of legislation to protect these rights. It is just that I do not believe that carrying out genetic research on a sample whose origin cannot be identified endangers or violates any of these rights or constitutes any personal risk to the persons from whom they were derived.

Knoppers and Laberge, in their commentary on the Clayton report, expressed similar feelings in a somewhat different manner.

> Access to residual tissues is essential to the understanding of disease, the development of new therapeutic modalities and tools, genetic epidemiology research to establish, for example, allele frequency in populations, and surveillance research to determine incidence and prevalence. This can be undermined by the sacralization of the sample. The anonymous-anonymized, altruistic contribution of the citizen to general well-being, the public health, and the advancement of science for the benefit of all members of a society is slowly being supplanted.
>
> Holding onto and controlling the physical or informatic destiny of human organs, gametes, embryos, tissues, blood and cells may at first glance seem the final, truly private, and personal stronghold of individual identify, privacy, and autonomy. Yet paradoxically, if carried too far, it may encourage the very reductionism that respect for individual integrity and human values as embodied in personal choices seeks to avoid. Samples even more than the human sources will take on a life, if not a legal personality, of their own. Anonymous or anonymized samples are sources, participants in human research are persons. (Knoppers and Laberge 1995, p. 1807)

What Are We Doing to Ourselves?

The controversy over informed consent for the analysis of stored tissue samples really started me thinking about what the genetics community is doing to itself, in trying to meet what it believes to be its ethical and social obligations. I would like to give you another example that raises the question of what are we doing to ourselves.

An editorial entitled "Crimes against Genetics" (1995) appeared in *Nature Genetics* just about the same time as the Maddox article. This title is, of course, a clever play on words, since the article dealt with the controversy surrounding a meeting held about a month earlier on the subject of "The Meaning and Significance of Research on Genetics and Criminal Behavior." The editorial broadly summarized the two sides of the dispute that surrounded the conference, as follows:

- On the side of the organizers, the goal was "to explore the implications of current genetic research of violent, antisocial and criminal behavior . . . to help to identify and aid those most likely to fall victim to sociological circumstances" (Crimes against Genetics 1995, p. 223).
- For the opponents, there was the fear "that these studies will lead only to the enslavement of the underclasses as social changes are abandoned in favor of easy-answer drug treatments or harsh restrictions on those deemed genetically irredeemable" (Crimes against Genetics, p. 223).

I am perhaps not the right person to analyze these two positions and to decide which, if either, is right and which is wrong. As a matter of fact, I think that there is considerable merit to some of the arguments about behavioral research, on both sides of the issue. However, I can understand, in the context of what I said earlier, how, as the editorialist put it, many of the behavioral scientists would feel "hurt at being so inaccurately depicted as racist or fascist" (Crimes against Genetics 1995, p. 224). It is the same way that I felt in some of the situations I described earlier.

But, how the behavioral scientists or other genetic researchers or I feel about what is said about our work really isn't the point of my concern. What troubles me is that there is or is starting to be a breakdown in our ability to engage in rational discourse about what genetic research is all about. For reasons that are certainly grounded in the history of the applications and misapplications of genetics, there is a movement to proscribe, to prohibit certain areas

of genetic research—because the findings or, perhaps more accurately, the potential applications of the findings are believed to be so frightening because of the possibilities for abuse. The editorial to which I referred, in paraphrasing the remarks of one of the speakers concerning the behavioral research controversy, puts it this way: "the public also sees scientific information, regardless of the soundness of the methods, as powerfully legitimizing, and, furthermore, the public's perception of genetic findings is that they are immutable. Thus the mere perception of reality (rather than the realities themselves) can provide impetus for the enactment of inequitable laws" (Crimes against Genetics 1995, p. 224).

There is a bit of a paradox here—although the public fears what genetics can do, it may uncritically accept what they think the geneticists are saying. And, it is not even the reality of what has been found. It's just the mere perception of reality. As I see it, this puts us geneticists in a tough position. On the hand, we need to be cognizant of these perceptions and of their power. On the other, we have to preserve the enterprise and to permit genetic research to move forward.

It is now time, after all of the stories I have told you and quotations I have shown, for me to summarize the message that I have been trying to present. As the present century is drawing to a close and a new one is about to begin, human genetics and its applied clinical science, medical genetics, are more powerful, rewarding, and exciting than ever. Progress has been enormous, and we have every reason to be proud of what we have been able to accomplish in such a remarkably short time. And yet we, the genetic researchers and practitioners, find ourselves in a disquieting situation. We are accused of engaging in too much hype about we think we know and are likely to be able to do, and we have been greeted by a considerable amount of equally—if not more—egregious hype from the opposing side. Not everyone trusts our motives or intentions, and, at the same time that the public is in awe of what we have already done, it fears what it thinks we might be able to do. We are very concerned about the social implications of what we have already done and will be able to do in the future. But in reacting to these concerns—our own concerns—we are in danger of tying ourselves in knots and of embracing policies and regulations that will only serve to impede the progress of human genetics, without necessarily protecting or enhancing the public good.

How should we deal with all of this? Two thousand years ago, the famous sage Rabbi Hillel (in the Pirke Avot 1:14) said: "If I am not for myself, who is for me? If I am only for myself, what am I? If not now—when?"

If I Am Not for Myself, Who Is for Me?

We, the human genetics research and clinical communities, need to stand up and make our case for what we have done, for what we are now doing, and for our future goals. We need to be strong advocates for our professions but must avoid claiming or promising too much ourselves or allowing others to make such claims in our names or on our behalf. We need to avoid conjuring up unfounded public fears and apprehensions by what we say. We need to work for regulations and legislation that, while preserving personal rights, enhance—rather than unnecessarily restrict—our ability to carry out research and to treat patients.

If I Am Only for Myself, What Am I?

While advocating our own position, the human genetics community must be ever mindful that we do not function in isolation and have responsibilities that transcend the purely professional. We need to educate the public, at every level, about what human genetics and geneticists are doing and hope to be able do. We must continue to be—and, if anything, become more—involved in the social and ethical debate that increasingly surrounds everything that we do. We need to be cognizant of the fact that we constitute just one element in the societal debate—which, hopefully, will be a rationale one—in the societal debate about the human applications of genetic knowledge. Important decisions about these applications certainly *will not* and *should not* be ours alone to make.

If Not Now—When?

The tension between scientific advance and societal concerns is not new, and it is certainly not unique to genetics. But the rapidity with which genetic information is being accumulated and new applications are being put forward makes the situation particularly acute for human genetics. The challenge facing human geneticists is to find the proper balance between the hopes and fears of society and the goals and interests our science—the discovery of new knowledge and the improvement of health and curing of disease. The challenge goes well beyond the weighing of issues at a conceptual level and extends to quite practical and important matters of control and regulation. This challenge must be faced by all of us, and it must be faced now!

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